

**REMARKS**

Claims 1-19 are pending in this application. Claims 3, 5-7 and 12-19 stand withdrawn.

As an initial matter, applicants respectfully request rejoinder of claims 3 and 5-7. In the previous Restriction Requirement, Group I encompassed all of compound claims, as written, based on Formula I. While the elected species did not read on all of the claims within Group I, Applicants' election of the elected species should not be read as a further limitation on the scope of Group I. Indeed, Applicants elected a species to which the claims would be limited if no generic claim were found allowable. The Examiner has offered no indication that the Examiner has required further restriction within Group I nor has the Examiner indicated that only a limited search was performed. As such, Applicants respectfully request rejoinder of claims 3 and 5-7 and full examination of the claims of Group I.

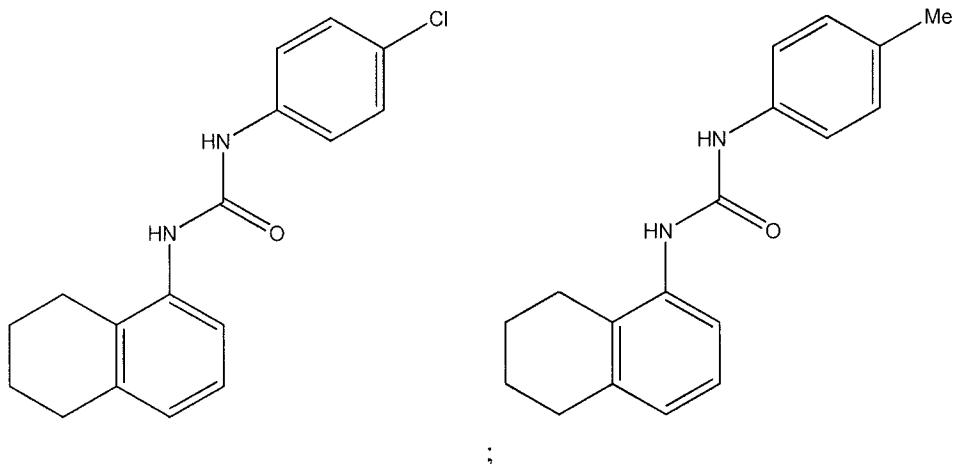
Nevertheless, Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is in condition for allowance.

**Rejections under 35 U.S.C. § 102(b)**

Claims 1-2,4 and 9-11 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by the English language abstract of Japanese Patent No. JP 4178362 ("JP '362").

The Examiner states that JP '362 discloses the following compounds which are encompassed by the instant claims ("A is unsubstituted, R1 is substituted or unsubstituted"):



Applicants respectfully disagree. The central urea moiety as instantly claimed is bound to the “A ring” moiety at the 2 position of the corresponding A ring. In the case of the compounds cited in JP ‘362, the corresponding A ring is a tetrahydronaphthalene moiety. Nevertheless, the central urea moiety of the cited compounds of JP ‘362 is bound to the 1 position of the tetrahydronaphthalene in each case.

Indeed, none of the compounds disclosed by JP ‘362 have a urea moiety bound to the 2 position of a tetrahydronaphthalene ring moiety. As such, Applicants respectfully assert that respectfully assert that JP ‘362 cannot anticipate the instant claims.

Applicants respectfully request that the rejections of the claims under 35 U.S.C. § 102(b) be withdrawn. As such, the rejection with respect to those claims is now moot.

#### Rejections under 35 U.S.C. § 103(a)

Claims 1-2,4 and 8-11 are rejected under 35 U.S.C. 103(a) as allegedly obvious in light of the English language abstract of Japanese Patent No. JP 4178362 (“JP ‘362”).

Specifically, the Examiner states that in view of JP ‘362 “it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to obtain compounds within the generic disclosure of the reference, because they are structurally so similar to those claimed in herein, with the reasonable expectation of achieving a successful composition, absent evidence to the contrary.” Applicants respectfully disagree.

To properly determine a *prima facie* case of obviousness, the Examiner “must step backward in time and into the shoes worn by the hypothetical ‘person of ordinary skill in the art’ when the invention was unknown and just before it was made.” M.P.E.P § 2142. This is important as “impermissible hindsight must be avoided and the legal conclusion must be gleaned from the prior art.” *Id.* Four factual inquiries must be made: first, a determination of the scope and contents of the prior art; second, a determination of the differences between the prior art and the claims in issue; third, a determination of level of ordinary skill in the pertinent art; and fourth, an evaluation of evidence of secondary consideration. *Graham v. John Deere*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966). Three criteria may be helpful in determining whether claimed subject matter is obvious under 103(a): first, if there is some suggestion or motivation to modify or combine the cited references; second, if there is a reasonable expectation of success; and third, if the prior art references teach or suggest all the claim limitations. *KSR Int'l Co. v. Teleflex, Inc.* No 04-1350 (U.S. Apr. 30, 2007). With regard to the first criterion, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.3d 690 (Fed. Cir. 1990). “Knowledge in the prior art of every element of a patent claim ... is not of itself sufficient to render claim obvious.” *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1333-34 (Fed. Cir. 2002)]. The issue is whether there is an apparent reason to combine the known elements in the fashion claimed by the patent at issue. *KSR Int'l Co. v. Teleflex, Inc.*

As stated above, the compounds of JP ‘362 differ from the claimed invention in that the urea moiety of the compounds of JP ‘362 is bound to the 1 position of the tetrahydronaphthalene in each case whereas the urea moiety of the claimed compounds is bound to the 2 position of the corresponding “A ring.”

Applicants respectfully submit that one of ordinary skill in the art would expect significantly different chemical properties (steric, electrochemical, pharmacological, etc) between compounds bearing a urea bound to the 1 position and compounds with a urea bound to the 2 position. Indeed, the reactivity of these two compounds is expected to be different as the substitution of different ring atoms will result in different substitution patterns. “In fused ring systems, the positions are not equivalent and there is usually a preferred orientation, even in the unsubstituted hydrocarbon” (March, *Advanced Organic Chemistry*, 6<sup>th</sup> ed. Wiley & Sons, 2007,

Page 674). For Example, “naphthalene is attacked [in electrophilic aromatic substitution] primarily at the 1 position by  $\text{NO}_2^+$ ,  $\text{NH}_2^-$ , and  $\text{PH}^\bullet$ ” (*Id.* at 676).

One or ordinary skill in the art would recognize that such differences, at a minimum, could dramatically affect the ability of the compounds to modulate the same receptors pharmacologically. As such, Applicants respectfully assert that one of ordinary skill in the art, at the time of the invention, would have lacked the motivation to modify the substitution position on the A ring of the instant compounds without potentially sacrificing the properties of the compounds.

Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. § 103.

**Non- Statutory Double Patenting**

Claims 1-2, 4 and 8-11 stand provisionally rejected on the grounds of non-statutory double patenting over claims 1-16 of copending U.S. Patent Application Serial No. 10/575,027 and over claims 1-5, 7 of copending U.S. Patent Application Serial No. 10/537,217.

As it remains unknown what subject matter claimed and disclosed in the present application will be deemed allowable; any statement regarding the provisional rejection made on Applicants’ part is premature. Therefore, Applicants respectfully traverse these rejections, and request that this rejection be held in abeyance until subject matter is deemed allowable in this application.

**CONCLUSION**

In view of the amendments and remarks made herein, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. Please charge any required fee or credit any overpayment to Deposit Account No. 04-1105.

Dated: January 26, 2009

Respectfully submitted,

Electronic signature: /Nicholas J. DiCeglie, Jr./  
Nicholas J. DiCeglie, Jr.

Registration No.: 51,615  
EDWARDS ANGELL  
PALMER & DODGE LLP  
P.O. Box 55874  
Boston, Massachusetts 02205  
(212) 308-4411  
Attorneys/Agents For Applicant  
Customer No. 35969